REMARKS

This submission is in response to the Official Action dated May 20, 2002. Claims 2 and 5-13 have been canceled, without prejudice or disclaimer. Claims 3 and 4 have been amended, and new claims 14-15 have been added. Thus, upon entry of this submission, claims 3-4 and 14-15 are pending.

The amendments have been made to expedite allowance of the application. Claim 3 has been amended to incorporate the subject matter of claim 2, and to recite a method of inducing cellular extensions. Support for this amendment can be found in the specification, *e.g.*, at page 4, lines 11-16.

New claim 14 recites a specific embodiment in which the cells are nerve cells. Support for this subject matter can be found, *e.g.*, page 6, lines 1-2, and in original claim 3.

New claim 15 recites that the cellular extensions terminate on distantly located cells. Support for this subject matter can be found on page 4, lines 11-16.

Reconsideration of the above identified application, in view of the above amendments and the following remarks, is respectfully requested.

Claim Rejections under 35 USC §112

35 U.S.C 112, First Paragraph - Written Description

Claims 2 and 4-5 have been rejected under section 112, first paragraph,

as failing to meet the written description requirement. Particularly, the Examiner contends that the specification fails to describe the structural requirements of a hNPRAP peptide comprising a C-terminal armadillo-like repeat or a biologically active hNPRPAP analogue.

As amended herewith, all claims, including new claim 14, recite a hNPRAP comprising the sequence of SEQ ID NO:4, thereby providing ample structural features of the hNPRAP used in the method of the invention. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

35 U.S.C. 112, First Paragraph - Enablement

Claims 1-5 have been additionally rejected for allegedly failing to comply with the enablement requirement. The Examiner contends that the specification fails to teach that neuronal cells respond to hNPRAP.

As amended, claim 3 calls for a method of inducing cellular extensions, as provided by specification (page 3, lines 2-5):

> ...Neural Plakophilin Related Armadillo Protein (NPRAP) – causes the development of numerous long, cellular extensions, which are similar to axonal sprouting observed during neuronal regeneration and synapse formation.

Hence, the specification explicitly teaches that hNPRAP induces cellular extensions of cells, that these cellular extensions typically terminate on distantly

located cells (specification, page 4, lines 11-16), and that hNPRAP stimulates nerve cell growth (page 5, lines 17-20) and neuronal regeneration (page 3, lines 12-15).

The specification further provides the hNPRAP gene is expressed as a range of transcripts in several regions of adult human brain, but is expressed at only very low levels in most non-neurologic tissues (page 5, lines 1-4), as well as the nucleotide and amino acid sequences of human NPRAP. Further described are methodologies of applying hNPRAP in various methods involving the induction of cellular extensions, such as stimulating nerve cell growth, and neuronal regeneration (see specification, *e.g.*, at page 3, lines 6-15; page 4, lines 11-16; page 5, lines 16-24; page 6, lines 1-8; and page 7, line 24to page 8, line 2).

It is noted that while one preferred embodiment of the method of the invention is the induction of cellular extensions of nerve cells, in particular synapse formation, the method of the invention as set forth by the amended claims is not restricted to nerve cells only. Indeed, the induction of cellular extensions ending on distantly located cells may apply to any cells type, including nerve cells. For example, the specification recites that assays for detecting axonal sprouting can be applied in neuronal cultures, and that dendrite formation may be tested in non-neurological cells using morphometric analyses which are well known in the art (page 7, lines 24-27).

From these descriptions , a person of ordinary skill in the art could

readily apply the human hNPRAP sequence in the experimental procedures described herein for inducing cellular extensions and neuronal regeneration, without undue experimentation.

Accordingly, since the invention is clearly enabled by the specification as filed, it appears that the Examiner is, instead, either doubtful as to the accuracy of the above statements in the specification, or as to whether all embodiments of the claims would be operable, *i.e.*, induce cellular extensions. For example, the Examiner cites Jackowski as supporting that neuronal cells are inhibited in regenerative capacity (Office Action, page 5, 1st paragraph), and states that the observed effects noted in the specification are generally displayed by a multitude of cells under various conditions, and that the noted effects in response to hNPRAP are not distinct among nerve cells, citing McDonald and other references (Office Action, page 5, 2nd paragraph).

More specifically, however, Jackowski, under the section "Conclusions", (page 311, 1st column) teaches as follows:

> It seems certain that CNS oligodendrocytes and myelin, possibly also PNS myelin, possess membrane- or extracellular matrix-associated molecules that inhibit the successful regeneration of adult mammalian CNS and PNS axons ... The lack of any significant regrowth of lesioned axons in CNS grey matter ... highlights also the inhibitory role of reactive astrocytes and a relative lack of neurotrophic molecules as being other important factors for CNS regeneration failure.

Thus, rather than providing any evidence that synapse formation or other

cellular extensions of nerve cells (or, indeed, of any cell) cannot be induced, Jackowski teaches that the actual formation may be inhibited by other factors, and that a lack of neurotrophic molecules may also be a crucial factor. This is not contrary to the statements in the specification, since Jackowski, nor any other reference cited by the Examiner, takes no issue with actual induction of neuronal growth or axon formation, only that various inhibitory events may occur, and indirectly suggests that the addition of neurotrophic factors could overcome these problems.

Similarly, the fact that cells may extend filopodia or other cellular extensions due to other reasons, as described in McDonald and other references, does nothing to render the instant invention any less enabled. The effect of hNPRAP on cells discovered by Applicants is a specific effect, as the cellular extensions are induced by contacting the cells with hNPRAP in an amount effective to cause cellular extensions. The claims recite these features.

Finally, any concern that the claims would read on inoperable embodiments does not offend §112, due to the following reasons.

> ...typically, inoperative embodiments are excluded by the language in a claim (*e.g.*, preamble)...MPEP 2164.08(b).

The pending claims are all directed to a method of inducing cellular extensions by contacting cells with an amount of hNPRAP effective to cause cellular

extensions. Accordingly, a functional result, which the specification teaches, is part of the claim, thus alleviating any concern the Examiner may have regarding inoperative embodiments.

Accordingly, it is respectfully submitted that the claims as amended herewith are fully enabled, and reconsideration and withdrawal of this rejection is therefore respectfully requested.

35 U.S.C. 112, Second Paragraph - Indefiniteness

Claims 2 and 4-5 have been rejected as allegedly being indefinite for failing to point out and distinctly claim the invention. The Examiner contends that the specification contains multiple descriptions of what can be "hNPRAP" and there is no guidance for the structure which is a peptide comprising a C-terminal armadillo-like repeat other than p0071 and β-catenin peptides.

As amended herewith, all claims, including new claim 14, recite that the hNPRAP used in the method of the invention comprises the sequence of SEQ ID NO:4, thereby providing a specific and definite description of the hNPRAP. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Claim Rejections under 35 U.S.C. §102

Claims 2 and 4-5 have been rejected as allegedly being anticipated by

Perez-Polo. The Examiner contends that the reference teaches multiple peptides that effect nerve cells and that the molecules that are disclosed in the reference can not be excluded from the generic recitation of hNPRAP.

As amended herewith, all claims, including new claim 14, recite a method of inducing cellular extensions by use of hNPRAP comprising the sequence of SEQ ID NO:4. Perez-Polo does not teach or suggest anything related to hNPRAP, the amino acid sequence of SEQ ID NO: 4[1], or any homolog or ortholog thereof.

Anticipation requires that each and every element of the rejected claim(s) be disclosed in a single prior art reference. See MPEP §2131. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

As such, Perez-Polo does not anticipate the claimed invention of amended claim 3 (as the Examiner indirectly recognized by not including that claim

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[1] It is noted that the hNPRAP (or, as it was previously called, "GT24" (see specification, page 4, lines 7-10)) sequence was previously known. For example, U.S. application Serial No. 08/888,077, filed July 3, 1997 and referred to on page 4, line 21of the specification, described the GT24 sequence, and a copy of the issued patent (U.S. Patent No. 6,020,143) was cited in Applicant's IDS of October 19, 2000. However, similar to Perez-Polo, the '143 patent does not teach or suggest methods of inducing cellular extensions, much less such methods using hNPRAP, or, indeed, any mammalian orthologs or homologs.

in the instant rejection) or any of the claims dependent thereon. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Conclusion

Therefore, in view of the above amendments and remarks, it is earnestly requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue.

If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Respectfully submitted,

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Peter H. ST. GEORGE-HYSLOP; Paul E. FRASER

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For: PROTEIN RELATED TO NEURONAL REGENERATION AND USES THEREOF

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November 7, 2002

3. (Amended) [The] A method [according to claim 2] of inducing cellular extensions, which method comprises contacting cells with a human Neural Plakophilin Related Armadillo Protein (hNPRAP) in an amount effective to cause cellular

extensions, wherein the hNPRAP [has] comprises an amino acid sequence as set forth in SEQ ID NO:4.

4. (Amended) The method according to claim [2] 14, wherein the [growth of nerve cells] contacting results in neuronal regeneration.

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